

# Recombinant DNA Permit Application



**Presentation to the Cambridge Biosafety Committee  
November 29, 2018**

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**790 Memorial Drive  
Suite 302  
Cambridge, MA 02139**

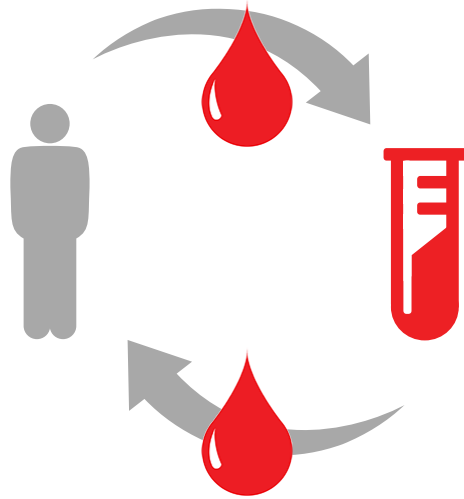
# Company Overview

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- Early-stage biotechnology company that will focus on the treatment of various genetic diseases including cancer
- Founded in 2018
- Number of employees: 8 and currently recruiting for 10 additional employees

# ElevateBio companies will benefit from industry-leading next gen cell and gene therapy manufacturing facility

## ElevateBio Aims to Become the World's Most Diversified Cell and Gene Therapy Portfolio by Leveraging Next Gen Manufacturing and Global Bench to Bedside Expertise



**elevateBIO Manufacturing**  
“The process is the product”

- Manufacture T-Cells, Stem Cells, Virus
- Accelerate product development timelines
- Increase POS in the clinic
- Reduce needle-to-needle time
- Reduce COGS
- Transform and save lives

# ElevateBio Founders

**David Hallal**



- Chairman and CEO, elevatelibio
- Former CEO, Alexion
- Former COO, CCO, Alexion
- Chairman, Scholar Rock
- Amgen, Biogen

**Vikas Sinha, MBA, CPA**



- CFO and Head of Strategy, elevatelibio
- Former CFO, Alexion
- Former Finance Executive, Bayer
- BOD member, Verona

**Ansbert Gadick, MD**



- Lead Investor and BOD, elevatelibio
- MPM Co-Founder & Managing Director
- Lead investor, Pharmasset, BioMarin, Radius
- Chairman, TCR<sup>2</sup> Therapeutics

**Mitch Finer, PhD**



- CSO, elevatelibio
- CEO, Oncorus; MPM Managing Director
- Former CSO, Bluebird Bio
- Cell and gene therapy pioneer

# Research Facility

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## Facility

Currently in two temporary spaces:

- 1 Main Street (office only)
- 790 Memorial Drive (office and lab) - approximately 3,800 sq. ft.

## Access Control

Locked building

One locked point of entry to office and laboratory space, access via keycard

## Lab Design

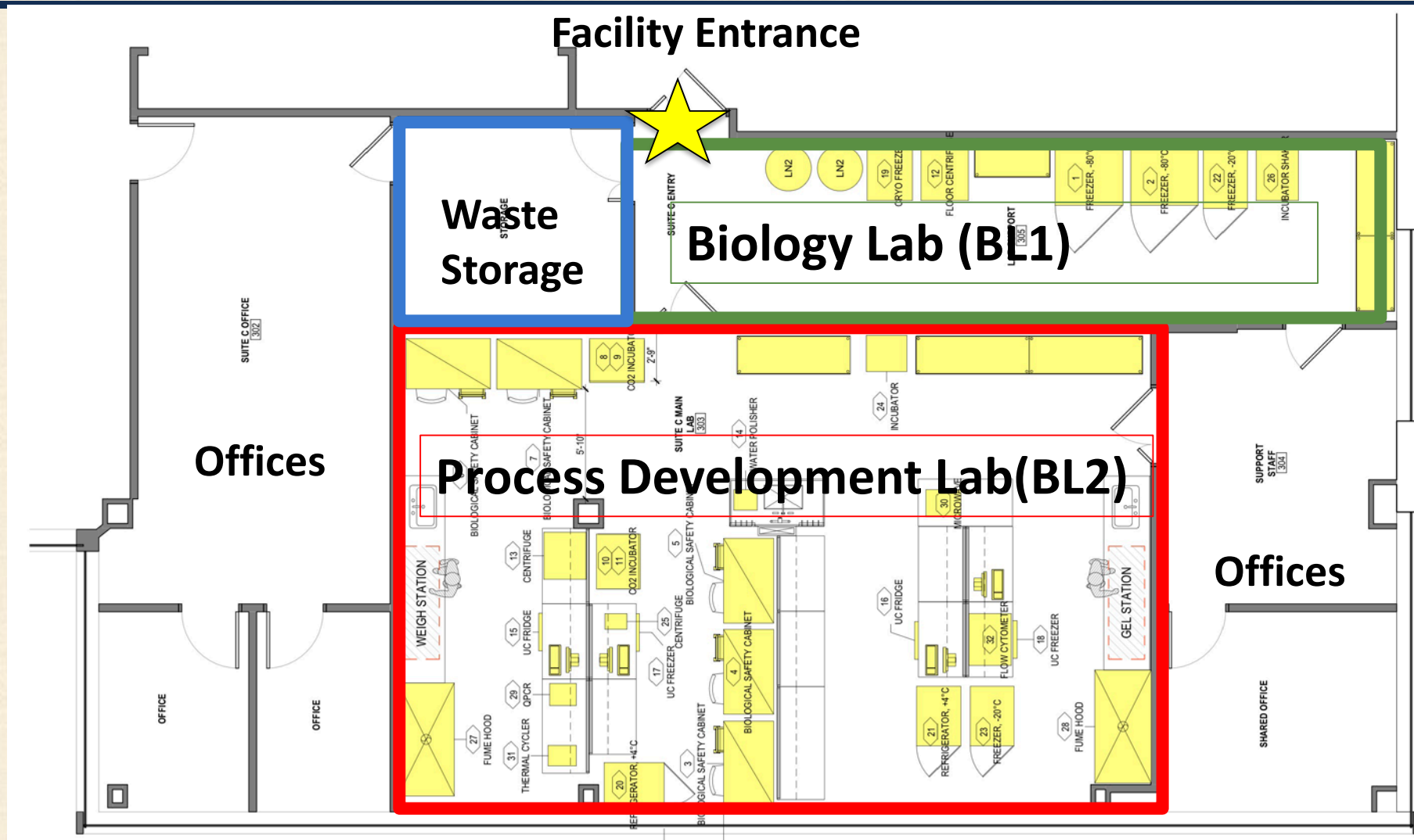
Main Biology laboratory (Proposed BL1)

Process Development laboratory (Proposed BL2)

Dedicated waste room for the storage of chemical and biological waste

Backflow prevention is in place

# 790 Memorial Drive Floor Plan



# Project Scope

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- Will generate viruses to be used as transfer vectors into immune and hematopoietic progenitor cells for the treatment various genetic diseases including cancer.
- Genes that will be modified will not be oncogenic or tumor suppressors.
- Human Immunodeficiency Virus (HIV-1) derived lentivirus and Moloney Murine Leukemia virus (MMLV) gamma retroviral vectors for the transfer of genes into various cell types such as T lymphocytes and autologous hematopoietic progenitor cells derived from peripheral blood or bone marrow.
- The lentiviral vectors that we will be using are 4<sup>th</sup> generation, self-inactivating virus that are produced using a multi-plasmid system that are designed to prevent recombination and the emergence of a replication competent virus.
- The plasmids for both viral vectors will be generated using molecular cloning techniques and the virus will be produced through either transient transfection of plasmid DNA into a cell line or use of a chemically inducible system from a stable cell line.

# Biosafety Levels 1 and 2

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- BSL1 containment appropriate for:
  - Plasmid expression systems
  - Bacterial hosts (e.g., *E coli*)
  - Non-toxic genes of interest (microRNA control sequences, metalloproteinase proteins, immune modulators, etc.)
  - PCR and other general lab procedures
- BSL2 containment appropriate for:
  - Human cells and cell lines
  - Lentivirus and retroviruses



# Biosafety Levels and Laboratory Policy

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## Proposed Biosafety Levels

- Process Development Lab (BL2)
- Biology Lab (BL1)
- Waste Storage Room (BL1)
- All lentiviral work will be contained in the biology lab

## PPE

- Safety glasses required in the tissue culture laboratory; gloves required for all benchwork
- Biology laboratory requires addition of buttoned lab coats

## Lab Safety

- Eating, drinking, and applying cosmetics is not permitted in and laboratory
- No gloves on any door handle
- Sharps are not permitted while using lentiviral vectors
- “Universal Precautions” used when handling human source material

# Safety Practices

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- Lentivirus and retroviruses are classified as Risk Group 2. All other materials used for the project, including human cell lines and tissue will be handled at BSL2.
- All work included in this project registration will be conducted according to the policies and procedures outlined in the Biosafety Manual and Exposure Control Plan, including but not limited to general handling, equipment use and waste procedures.
- A dedicated biosafety cabinet (decontaminated after each use) and incubator will be used.
- Sharps will be used only if essential.
- Gloves, lab coats and safety glasses will be worn for all virus work.
- When centrifuging, rotors/safety cups will be loaded/unloaded within the BSC.
- Liquid waste will be decontaminated with a final concentration of 10% bleach, 30 minute contact time.
- Lentivirus and retrovirus-specific safety training will be provided.

# ElevateBio Biosafety Program

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Described in Biosafety Manual/Exposure Control Plan prepared in November 2018

- Initial training within the first two weeks of hire
- Annual safety training
- Engineering controls (e.g., Class II biosafety cabinets)
- Personal protective equipment (safety glasses, lab coat, gloves required for all laboratory work in BL2)
- Safe work practices (hand washing, no eating/drinking, work surface decontamination)
- Medical surveillance (Mt. Auburn Occupational Health)
- Employees at risk of an occupational exposure to bloodborne pathogens (BBPs) are offered the Hepatitis B vaccination series and/or titer at the time of hire
- Emergency response and exposure control protocols are outlines in the Biosafety Manual and Exposure Control Plan and the Emergency Action Plan.

# Elevatebio Base Camp

## 790 Memorial Drive

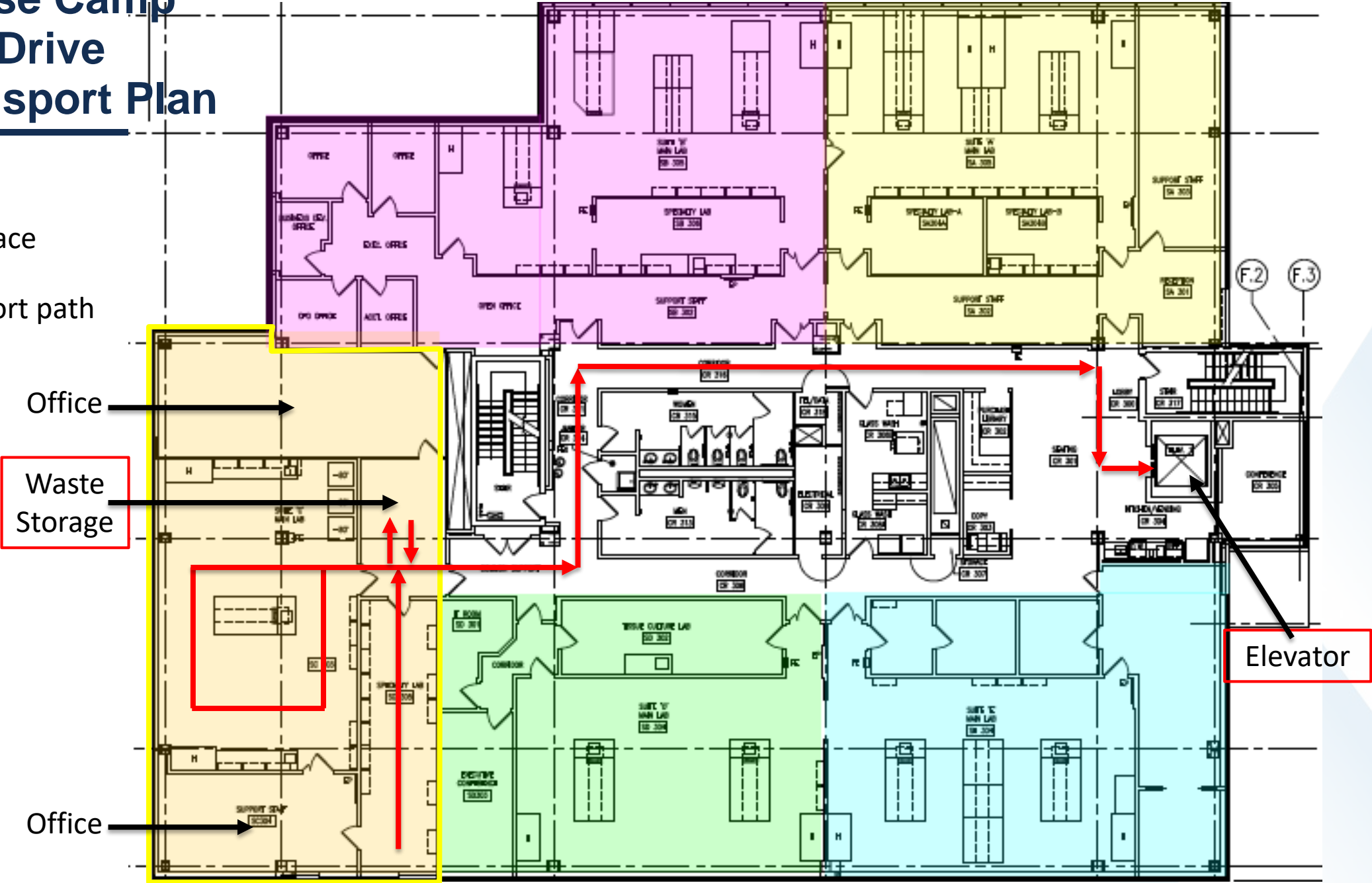
### Biowaste Transport Plan



Elevatebio space



Waste transport path



# Biological Waste

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- Liquid biological waste from virus studies, and other biological work, will be decontaminated with freshly prepared 10% bleach for 30 minute contact time, prior to sink disposal
- Solid biological waste will be collected in bioboxes
- Sharps are collected in rigid, puncture resistant containers
- All waste is sealed in the respective laboratory prior to being moved into the waste storage area
- Solid biological waste and sharps will be stored in a designated/posted waste room for pick-up by Stericycle
- No waste is taken into common space without being completely sealed

# Institutional Biosafety Committee

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- The Elevatebio Base Camp IBC will review all work involving rDNA and potentially infectious biological material
- No rDNA work will be conducted prior to permit approval by the CBC and satisfactory lab walkthrough; review and approval of project registration by the IBC
- IBC membership is comprised of five members, including two community representatives (both Cambridge residents)
- IBC met on November 12, 2018; protocol approved

# Permits and Timeline

Permit	Agency	Status	Permit Holder
rDNA	Cambridge Public Health Department	In-progress	Elevatebio Base Camp
Wastewater	MWRA	Complete	Landlord – Alexandria Real Estate
Flammables Storage	Cambridge Fire Department	In-progress	Elevatebio Base Camp
VSQG Hazardous Waste Registration	Massachusetts DEP	In-progress	Elevatebio Base Camp

# Contracts

Permit	Vendor	Status
Biological Waste/Sharps Disposal	Stericycle	Complete
Hazardous Waste Disposal	Veolia	In-progress
Lab Coat Services	Unifirst	In-progress
Occupational Health	Mount Auburn Hospital	Complete
Fume Hood/BSC Certification	Air Systems Tech	In-progress
Pest Control Services	Waltham Pest Control	Complete
Safety Consultants	Safety Partners	Complete